

What is Claimed is:

1. A method for diagnosing Bloom's syndrome in a subject comprising detecting the presence of two mutated *BLM* genes or the absence of a wild type *BLM* gene in nucleic acid
5 of the subject.
2. The method of Claim 1 wherein the subject is an embryo, fetus, newborn, infant or adult.
3. The method of Claim 1 wherein each mutated *BLM* gene has one or more deletion, insertion, point or
10 rearrangement mutations.
4. The method of Claim 1 wherein the nucleic acid is DNA or RNA.
5. The method of Claim 1 wherein the presence of the mutated *BLM* genes or the absence of the wild type *BLM*
15 gene is detected by one or more techniques selected from the group consisting of sequence analysis, restriction enzyme digestion analysis, hybridization and polymerase chain reaction.
6. The method of Claim 1 wherein the presence of the mutated *BLM* genes or the absence of the wild type *BLM*
20 gene is detected by the presence of a gene product encoded by each mutated *BLM* gene or the absence of a gene product encoded by the wild type *BLM* gene.
7. The method of Claim 6 wherein the gene product
25 is a protein.
8. The method of Claim 7 wherein the protein is detected by immunoblotting, immunoprecipitation, solid phase radioimmunoassay, or enzyme-linked immunoabsorbent assay.
9. The method of Claim 6 wherein the gene product
30 is mRNA.
10. The method of Claim 9 wherein the mRNA is detected by one or more techniques selected from the group consisting of sequence analysis, restriction enzyme digestion analysis, hybridization and polymerase chain reaction.

11. A method for determining whether a subject is a carrier of a mutated *BLM* gene comprising detecting the presence of a mutated *BLM* gene in nucleic acid of said subject.

5 12. The method of Claim 11 wherein the subject is an embryo, fetus, newborn, infant or adult.

13. The method of Claim 11 wherein the mutated *BLM* gene has one or more deletion, insertion, point or rearrangement mutations.

10 14. The method of Claim 11 wherein the nucleic acid is DNA or RNA.

15 15. The method of Claim 11 wherein the presence of the mutated *BLM* gene is detected by one or more techniques selected from the group consisting of sequence analysis, restriction enzyme digestion analysis, hybridization and polymerase chain reaction.

16. The method of Claim 11 wherein the presence of the mutated *BLM* gene is detected by the presence of a gene product encoded by the mutated *BLM* gene.

20 17. The method of Claim 16 wherein the gene product is a protein.

25 18. The method of Claim 17 wherein the protein is detected by immunoblotting, immunoprecipitation, solid phase radioimmunoassay, enzyme-linked immunoabsorbent assay or western blotting.

19. The method of Claim 16 wherein the gene product is mRNA.

30 20. The method of Claim 19 wherein the mRNA is detected by one or more techniques selected from the group consisting of sequence analysis, hybridization and polymerase chain reaction.

21. A single-stranded nucleic acid probe which specifically hybridizes to wild type *BLM* nucleic acid.

35 22. The probe of claim 21 which is labeled with a detectable marker.

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38. A kit useful for detecting a wild type *BLM* protein comprising an antibody immunoreactive with the wild type *BLM* protein.

39. A kit useful for detecting a mutant *BLM* protein comprising an antibody immunoreactive with the mutant *BLM* protein.

40. A kit useful for detecting a wild type *BLM* protein and a mutant *BLM* protein comprising an antibody immunoreactive with the wild type *BLM* protein and an antibody immunoreactive with the mutant *BLM* protein.

41. A method for treating or preventing the onset of Bloom's syndrome in a subject in need of such treatment or prevention comprising the delivery and expression of a functional *BLM* gene into a sufficient number of cells of the subject to treat or prevent the onset of Bloom's Disease in the subject.

42. The method of Claim 41 wherein the subject is an embryo, fetus, newborn, infant or adult.

43. The method of Claim 41 wherein the functional *BLM* gene is delivered by homologous recombination.

44. The method of Claim 41 wherein the functional *BLM* gene is delivered by a vector.

45. The method of Claim 44 wherein the vector is a viral vector.

46. The method of Claim 45 wherein the viral vector is a retrovirus.

47. The method of Claim 45 wherein the viral vector is a DNA virus.

48. The method of Claim 41 wherein the functional *BLM* gene is delivered by transfection.

49. A recombinant viral vector for treating a defect in the *BLM* gene in a target cell comprising (a) the nucleic acid of or corresponding to at least a portion of the genome of a virus, which portion is capable of directing the infection of the target cell, and (b) a functional *BLM* gene

operably linked to the viral nucleic acid and capable of being expressed as a functional gene product in the target cell.

50. The recombinant viral vector of Claim 49 which
5 is a retrovirus.

51. The recombinant viral vector of Claim 49 which is a DNA virus.

52. A stem cell which expresses the functional *BLM* gene introduced therein through viral transduction.

10 53. A stem cell which expresses the functional *BLM* gene introduced therein through homologous recombination.

54. A stem cell which expresses the functional *BLM* gene introduced therein through transfection.

15 55. A purified and isolated nucleic acid encoding an enzymatically active *BLM* protein.

56. The nucleic acid of Claim 55 wherein the *BLM* protein is the wild type protein or an analogue thereof.

57. The nucleic acid of Claim 55 which is genomic DNA, cDNA or RNA.

20 ✓ 58. The nucleic acid of Claim 55 encoding the amino acid sequence contained in Figure 2.

59. The nucleic acid of Claim 55 having the nucleotide sequence contained in Figure 2.

25 60. A vector comprising a nucleic acid encoding an enzymatically active *BLM* protein.

61. The vector of Claim 60 wherein the *BLM* protein is the wild type protein or an analogue thereof.

62. The vector of Claim 60 wherein the nucleic acid encodes the amino acid sequence contained in Figure 2.

30 ✓ 63. The vector of Claim 60 wherein the nucleic acid has the nucleotide sequence contained in Figure 2.

64. A cell stably transformed with a vector comprising a nucleic acid encoding an enzymatically active *BLM* protein.

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65. The cell of Claim 64 wherein the BLM protein is the wild type protein or an analogue thereof.

66. The cell of Claim 64 wherein the nucleic acid encodes the amino acid sequence contained in Figure 2.

5 67. The cell of Claim 64 wherein the nucleic acid has the nucleotide sequence contained in Figure 2.

68. The cell of Claim 64 which is eukaryotic.

69. The cell of Claim 64 which is prokaryotic.

10 70. A method for producing a recombinant, enzymatically active BLM protein comprising culturing a cell transformed with a vector comprising a nucleic acid encoding an enzymatically active BLM protein, and recovering BLM protein from the culture.

15 71. The method of Claim 70 wherein the BLM protein is the wild type protein or an analogue thereof.

72. The method of Claim 70 wherein the nucleic acid encodes the amino acid sequence contained in Figure 2.

73. The method of Claim 70 wherein the nucleic acid has the nucleotide sequence contained in Figure 2.

20 74. The method of Claim 70 wherein the cell is eukaryotic.

75. The method of Claim 70 wherein the cell is prokaryotic.

76. A purified, enzymatically active BLM protein.

25 77. The protein of Claim 76 which is the wild type protein or an analogue thereof.

78. The protein of Claim 76, which is recombinantly produced.

30 79. The protein of Claim 76 which has the amino acid sequence contained in Figure 2.

80. A vector comprising a mutated *BLM* gene which is capable of introducing the mutated *BLM* gene in at least some embryonic cells to which the vector is introduced.

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81. An embryonic stem cell comprising a mutated *BLM* gene which has been integrated into the cell following transduction with the vector of Claim 80.

82. A non-human, transgenic animal comprising a
5 mutated *BLM* gene.

83. The non-human, transgenic animal of Claim 82 whose germ and somatic cells contain a mutated *BLM* gene sequence introduced into said animal, or an ancestor thereof, at an embryonic stage.

10 84. The non-human, transgenic animal of Claim 83
whose germ and somatic cells do not contain a wild type *BLM*
gene.

85. A method of producing a non-human, transgenic animal comprising introducing a mutated *BLM* gene into at least some cells of a recipient, non-human animal.